

Does the EPR signal of nitric oxide-ferro-dithiocarbamate complex prove the existence of genuine NO?

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Despite their widespread use as spin trap agents for nitric oxide detection, the chemical properties of iron-dithiocarbamate complex are unknown. The object of our study is to clarify the redox chemistry of water-soluble iron complexes with N-methyl-D-glucamine dithiocarbamate (MGD). Under aerobic condition, $\text{Fe}^{2+}(\text{MGD})_2$ complex is rapidly oxidized by dissolved oxygen to form the $\text{Fe}^{3+}(\text{MGD})_3$ complex with a rate of $5 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$, followed by the formation of reactive oxygen species (ROS), such as superoxide anion radical, hydrogen peroxide and hydroxyl radical.¹⁾ The $\text{Fe}^{2+}(\text{MGD})_2$ complex also acts as a one-electron reductant of nitrite and nitrosogluthione. The reduction rate for nitrite is relatively slow ($4.8 \text{ M}^{-1} \text{ s}^{-1}$) though, incubation of nitrite with $\text{Fe}^{2+}(\text{MGD})_2$ complex may still cause the overestimation of NO production.²⁾ Physiologically dominant thiol compounds such as glutathione and cysteine accelerate the formation of NO- $\text{Fe}^{2+}(\text{MGD})_2$ complex through the reduction of the oxidized iron-MGD complex ($\text{Fe}^{3+}(\text{MGD})_3$) in the presence of nitrite. Furthermore, depletion of glutathione was demonstrated in cultured PC12 cells, and thiol compounds enhanced the formation of ROS by accelerating its turnover. Nitrosogluthione spontaneously reacted with $\text{Fe}^{2+}(\text{MGD})_2$ complex with a 1:2 stoichiometry. In fact, $\text{Fe}^{2+}(\text{MGD})_2$ complex is as good an indicator of nitrosothiols as it is of NO. These results elucidate the difficulties of utilizing the $\text{Fe}^{2+}(\text{MGD})_2$ complex for the quantitation of NO in biological samples, especially in vivo.

1) Tsuchiya K, Jiang JJ, Yoshizumi M, Tamaki T, Houchi H, Minakuchi K, Fukuzawa K, Mason RP. Nitric oxide-forming reactions of the water-soluble nitric oxide spin-trapping agent, MGD. *Free Radic Biol Med.* 27(3-4), 347-355, 1999. 2) Tsuchiya K, Yoshizumi M, Houchi H, Mason RP. Related Articles Nitric oxide-forming reaction between the iron-N-methyl-D-glucamine dithiocarbamate complex and nitrite. *J Biol Chem.* 275(3), 1551-1556, 2000.